

(19) World Intellectual Property
Organization
International Bureau



16 MAY 2005

(43) International Publication Date
22 April 2004 (22.04.2004)

PCT

(10) International Publication Number
WO 2004/033425 A1

(51) International Patent Classification⁷: C07D 207/16,
A61K 31/40, A61P 31/14

(21) International Application Number:
PCT/IB2003/004884

(22) International Filing Date: 9 October 2003 (09.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
02292487.2 9 October 2002 (09.10.2002) EP

(71) Applicant (for all designated States except US): GENO-
SCIENCE [FR/FR]; 25 et 27, rue de Friedland, F-13006
Marseille (FR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HALFON, Philippe
[FR/FR]; 11, allée du Prado Bleu, F-13008 Marseille (FR).
SAYADA, Chalôm [FR/LU]; 22, rue Marie Adélaïde,
L-2124 Luxembourg (FR). FERYN, Jean-Marc [FR/FR];
Domaine du Rian Séjour, Traverse de la Pignatelle,

F-13012 Marseille (FR). PERBOST, Régis [FR/FR];
3, boulevard de la Corderie, F-13007 Marseille (FR).
GARZINO, Frédéric [FR/FR]; 20, Bd. Gillibert,
F-13009 Marseille (FR). CAMPLO, Michel [FR/FR];
14, Boulevard A. Aune, F-13006 Marseille (FR). COUR-
CAMBECK, Jérôme [FR/FR]; 15, rue d'Isly, F-13005
Marseille (FR). PEPE, Gérard [FR/FR]; Les Severiers,
24, allée du Paradou, F-13600 La Ciotat (FR).

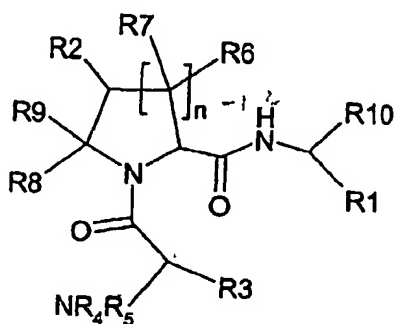
(74) Agents: BECKER, Philippe et al.; Cabinet Becker et As-
sociés, 35 rue des Mathurins, F-75008 Paris (FR).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT,
RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

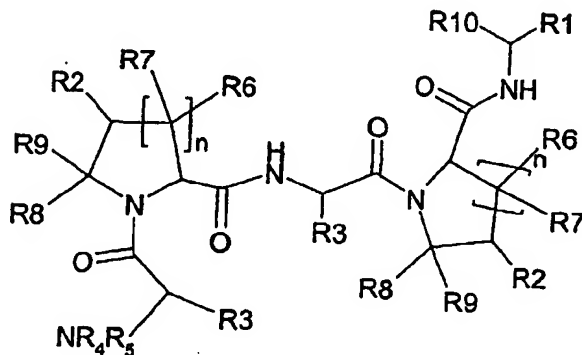
(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,

[Continued on next page]

(54) Title: PYRROLIDINE DERIVATIVES FOR USE IN TREATING HEPATITIS C VIRUS INFECTION



(I)



(II)

(57) Abstract: The present invention relates to novel hepatitis C virus ("HCV") protease inhibitors or other flavivirus protease inhibitors having the general structure (I) or (II), pharmaceutical compositions containing one or more such inhibitors, methods for preparing such inhibitors, uses of these compounds to treat hepatitis C and related disorders together with their use for their activity towards NS3 serine protease, intermediary compounds for the method of preparation of said compounds and screening methods. The invention specifically discloses novel chemical compounds as inhibitors of the HCV serine protease.

WO 2004/033425 A1



ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/04884

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D207/16 A61K31/40 A61P31/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT.

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02 48172 A (SCHERING CORP) 20 June 2002 (2002-06-20) claims; examples	1-25
Y	WO 00 09543 A (BOEHRINGER INGELHEIM CA LTD ;GOUDREAU NATHALIE (CA); GHIRO ELISE () 24 February 2000 (2000-02-24) claims; examples	1-25
Y	WO 02 08198 A (SCHERING CORP) 31 January 2002 (2002-01-31) page 19 -page 20; examples; tables 2,4	1-25
Y	WO 00 59929 A (BOEHRINGER INGELHEIM CA LTD ;GOUDREAU NATHALIE (CA); GHIRO ELISE () 12 October 2000 (2000-10-12) examples 21,23,25	1-25

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

13 February 2004

Date of mailing of the international search report

02/03/2004

Name and mailing address of the ISA

European Patent Office, P.B. 6818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3018

Authorized officer

Menegaki, F

INTERNATIONAL SEARCH REPORT

International Application No
PC1/IB 03/04884

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0248172	A	20-06-2002	AU 3659102 A	24-06-2002
			CA 2430458 A1	20-06-2002
			EP 1343807 A2	17-09-2003
			HU 0303436 A2	28-01-2004
			WO 0248172 A2	20-06-2002
			US 2002147139 A1	10-10-2002
WO 0009543	A	24-02-2000	AU 5273199 A	06-03-2000
			BG 105232 A	30-11-2001
			BR 9913646 A	05-06-2001
			CA 2338946 A1	24-02-2000
			CA 2445938 A1	24-02-2000
			WO 0009543 A2	24-02-2000
			CN 1323316 T	21-11-2001
			CZ 20010516 A3	15-08-2001
			EA 3906 B1	30-10-2003
			EE 200100081 A	15-08-2002
			EP 1105413 A2	13-06-2001
			HR 20010102 A1	28-02-2002
			HU 0105144 A2	29-04-2002
			ID 27839 A	26-04-2001
			JP 2002522554 T	23-07-2002
			NO 20010683 A	02-04-2001
			PL 346626 A1	25-02-2002
			SK 2062001 A3	08-10-2001
			TR 200100432 T2	21-09-2001
			TR 200200129 T2	21-06-2002
			US 6534523 B1	18-03-2003
			US 6323180 B1	27-11-2001
			US 6268207 B1	31-07-2001
			US 6329379 B1	11-12-2001
			US 6329417 B1	11-12-2001
			US 2002016442 A1	07-02-2002
			US 2002037998 A1	28-03-2002
WO 0208198	A	31-01-2002	AU 8292201 A	05-02-2002
			CA 2410766 A1	31-01-2002
			EP 1301486 A2	16-04-2003
			WO 0208198 A2	31-01-2002
			US 2002102235 A1	01-08-2002
WO 0059929	A	12-10-2000	AU 3548000 A	23-10-2000
			BG 105970 A	31-05-2002
			BR 0009599 A	15-01-2002
			WO 0059929 A1	12-10-2000
			CA 2367127 A1	12-10-2000
			CN 1346365 T	24-04-2002
			CZ 20013467 A3	12-06-2002
			EE 200100516 A	16-12-2002
			EP 1169339 A1	09-01-2002
			HR 20010720 A1	31-12-2002
			HU 0300121 A2	28-06-2003
			ID 30459 A	06-12-2001
			JP 2002542160 T	10-12-2002
			NO 20014857 A	31-10-2001
			PL 350855 A1	10-02-2003
			SK 14072001 A3	05-03-2002
			TR 200102878 T2	21-01-2002

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB 03/04884

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0059929	A	US 2004002448 A1 US 6608027 B1	01-01-2004 19-08-2003